

## REMARKS

### I. Status Summary

Claims 1, 7, 8, and 28-30 are pending in the present U.S. patent application and have been examined by the United States Patent and Trademark Office (hereinafter "the Patent Office") in a Non-Final Official Action dated April 14, 2009 (hereinafter "the Non-Final Official Action").

Claims 1, 7, 8, and 28-30 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims are not enabled over their full scope.

Claim 7 has been canceled without prejudice. Applicants respectfully reserve the right to file one or more continuation and/or divisional applications with claims directed to the subject matter of the canceled claim.

Claims 1 and 28 have been amended. Certain of the amendments are formal in nature (e.g., amending "presented" to "present" in claims 1 and 28), and thus no new matter has been added by these amendments. Support for the additional amendment to claim 1 can be found throughout the specification as filed, including particularly in Figure 1 as filed and in the description accompanying Figure 1 at page 5, lines 13-17 (absorption site is at the intestinal epithelium). Additional support can be found at page 8, lines 5-8, and at page 9, lines 9-16 (absorption site is at the blood-brain barrier). Thus, no new matter has been added by the amendment to claim 1.

Reconsideration of the application based on the application as amended and in light of the remarks set forth below is respectfully requested.

### II. Response to the Rejection under 35 U.S.C. § 112, First Paragraph

Claims 1, 7, 8, and 28-30 have been rejected under 35 U.S.C. § 112, first paragraph, upon the contention that the claims are not enabled over their full scope. According to the Patent Office, the claims are enabled for enhancing paracellular permeability in the intestinal epithelium or the blood-brain barrier, but are not enabled for enhancing paracellular permeability at an absorption site, generally, or for determining at what "time" the effect is desired.

After careful consideration of the rejection and the Patent Office's basis therefor, applicants respectfully traverse the rejection and submit the following remarks.

Initially, claim 7 has been canceled without prejudice, and thus the instant rejection is believed to be moot as to claim 7.

Continuing, with respect to the Patent Office's assertions regarding determining at what "time" the effect is desired, applicants respectfully submit that the Patent Office has not presented any arguments as to why one of ordinary skill in the art would have needed to employ undue experimentation to determine at what time increasing paracellular permeability would be desired. As such, applicants respectfully submit that the Patent Office has not presented a *prima facie* case of lack of enablement with respect to this element.

Nonetheless, applicants respectfully submit the following remarks with respect to this element. Applicants respectfully submit that "a time in which enhanced paracellular permeability is desired" would be understood by one of ordinary skill in the art after consideration of the instant specification. For example, the specification as filed discloses that there is an ongoing difficulty in treating subjects with certain drugs that are poorly absorbed across the intestinal epithelium and the blood-brain barrier. As set forth on pages 2-3 of the instant specification, compounds that can easily partition into the lipid bilayer of the cell membrane are generally easily absorbed. Hydrophilic compounds, in contrast, are substantially unable to cross the cell membrane. Their passage across the intestinal epithelium or the blood-brain barrier via the intercellular route (paracellular route) is also severely restricted by the presence of intercellular junctions, known as tight junctions.

Therefore, applicants respectfully submit that upon a review of the instant disclosure, one of ordinary skill in the art would understand that the presence of tight junctions would negatively impact the bioavailability of certain medications. In order to increase the bioavailability of such medications, enhancing paracellular permeability across the tight junctions would be desirable. Applicants respectfully submit, therefore, that upon a review of the instant disclosure, one of ordinary skill in the art would recognize that enhanced paracellular permeability for poorly absorbed medications would be desired at the time the medication is administered, during the time interval during which the medication travels to the absorption site (e.g., as it travels through the gastrointestinal tract and/or through the blood stream), and/or as it is traversing the tight

junctions at the absorption site. Applicants respectfully submit that this would be a routine consideration by one of ordinary skill in the art upon a review of the instant disclosure, and thus there is believed to be no basis for the Patent Office to assert that it would require undue experimentation for one of ordinary skill in the art to determine the time at which the effect would be desired.

As a result, applicants respectfully submit that the Patent Office's assertion that determining at what "time" the effect is desired would require undue experimentation is unsubstantiated and fails to support the instant rejection.

Turning now to the Patent Office's contention that the claims are not enabled for enhancing paracellular permeability at an absorption site other than the intestinal epithelium or the blood-brain barrier, applicants respectfully submit that claim 28 as currently pending already recites "enhancing paracellular permeability in the subject in the intestinal epithelium...where tight junctions are present". As such, applicants respectfully submit that claim 28 is believed to be fully enabled.

With respect to claim 1, applicants have amended claim 1 to recite *inter alia* a method of enhancing paracellular permeability at an absorption site in a subject through the administering of the effective amount of the phospholipase C inhibitor, wherein the absorption site is a site in the intestinal epithelium or in the blood-brain barrier of the subject. As such, and in light of the Patent Office's acknowledgement that the claims are enabled for enhancing paracellular permeability in the intestinal epithelium or the blood-brain barrier, applicants respectfully submit that claim 1 as amended is fully enabled.

Accordingly, applicants respectfully submit that independent claims 1 and 28 are believed to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. Claims 8, 29, and 30 depend from claim 1 or from claim 28, and thus are also believed to comply with the enablement requirement of 35 U.S.C. § 112, first paragraph. As a result, applicants respectfully submit that claims 1, 8, and 28-30 are in condition for allowance, and respectfully solicit a Notice of Allowance to that effect.

CONCLUSION

In light of the above amendments and remarks, it is respectfully submitted that the present application is now in proper condition for allowance, and an early notice to such effect is earnestly solicited.

If any small matter should remain outstanding after the Patent Examiner has had an opportunity to review the above Remarks, the Patent Examiner is respectfully requested to telephone the undersigned patent attorney in order to resolve these matters and avoid the issuance of another Official Action.

DEPOSIT ACCOUNT

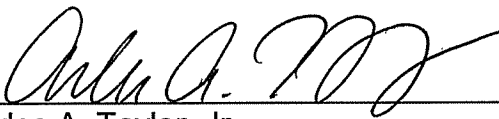
Although no fee is believed to be due with respect to the filing of the instant paper, the Commissioner is hereby authorized to charge any underpayment of fees, and to credit any over payment, to Deposit Account Number 50-0426.

Respectfully submitted,

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Date: August 14, 2009

By: \_\_\_\_\_



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